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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,265	11/28/2000	Bruce Marvin Held	N1205-008	7900
32905	7590	11/19/2003		
JONDLE & ASSOCIATES P.C. 9085 EAST MINERAL CIRCLE SUITE 200 CENTENNIAL, CO 80112				
EXAMINER HELMER, GEORGIA L				
ART UNIT		PAPER NUMBER		
1638				

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,265	HELD ET AL.	
	Examiner	Art Unit	
	Georgia L. Helmer	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,7-16,18-20,56-61 and 63-65 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,7-16,18-20,56-61 and 63-65 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

Status of the Claims

1. The Office acknowledges receipt of Applicants Response; dated July 31,2003.
2. Applicant has cancelled claim 17, and amended claim 1. Claims 1, 2, 3, 7-16, 18-20, 56-61 and 63-65 are pending, and are examined in the instant action.
3. The Office acknowledges receipt of the 1.132 Declaration of Dr. Herbert Martin Wilson.
4. This action is made FINAL necessitated by Applicant's amendment.
5. All rejections not addressed below have been withdrawn.
6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102/103

7. Claims 1,2, 4, 7-10, 13-16 , 18-20, 56-57, 61, and 63 remain rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Mets, US 5,240,842, issued August 31, 1993, for reasons of record, which are reiterated below:

Mets teaches a method of introducing molecules into a plant cell (Abstract, for example), comprising preparing a solution of nucleic acid (Abstract), supplying the solution for conversion to aerosol droplets at a flow rate (Abstract), producing aerosol

Art Unit: 1638

droplets comprising the nucleic acid, accelerating the droplets toward the cell, and impacting the cell with the droplets (Claim 1 (c) and (d)), where the molecules are nucleic acid (claim 2), where the cell is a plant cell (Abstract), where the plant cell is a corn cell (claim 4), where the aerosol droplets are less than 0.1 micron in diameter (col 5, lines 20-22; claim 3), where the droplets are continuously targeted, where the target surface can be controlled, where the nucleic acid is a vector (col 11/lines 22-30), the use of a microflow nebulizer (col 8, lines 60-65), regenerating a transgenic plant (col 3, line 67), and progeny of the plant (col 4, line 2).

Claims 1,2, 4, 7-10, 13-16, 18-20, 56-57, 61, and 63 require limitations of a flow rate which has the property or characteristic of being various rates between 1 microliter/minute to 350 microliter/minute. Mets teaches introducing molecules into a cell as claimed in the instant invention but does not recite any specific flow rate. The Examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property, since the Mets patent is silent on aerosol flow rates. However, the method of Mets used an aerosol flow rate which enabled the introduction of nucleic acids into a plant cell. With these conditions, where the method seems to be identical except that the prior art is silent to the characteristic or property claimed, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. See *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Accordingly, Mets anticipates the claimed invention.

Claim Rejections - 35 USC § 103

8. Claims 1,2, 4, 7-10, 13-16, 18-20, 56-58, 60, 61, and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mets as discussed above, and further in view of Pui, et al, WO 98/56894, publication date 17 December 1998.

Mets teaches the claimed method of introducing a molecule into a plant cell, as stated above. Mets does not specifically teach an aerosol flow rate or 1 microliter/minute to 350 microliters/minute. Pui teaches flow rates of "about 0.01 microliter/minute to about 5 microliters/minute" (p 36, lines 2-3) in a method of introducing a molecule into a cell. The Office interprets 8 microliters/minutes to be "about 5 microliters/minute".

Given the recognition of one of ordinary skill in the art, of the value of introducing a nucleic acid molecules into a plant cell, as taught by Mets, one of ordinary skill in the art would have been motivated to used the specific flow rates taught by Pui for the introduction of nucleic acids into a cell. Thus the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary. Accordingly, the claimed invention is prima facie obvious in view of the prior art.

The Declaration of Herbert Martin Wilson, PhD.

The Declaration of Herbert Martin Wilson, PhD. ("the Declaration") has been thoroughly considered and is found nonpersuasive.

9. In the Declaration, Applicant says that he "has described the rates used by Mets, the results as they relate to flow rate, and why the present invention represents an

unexpected improvement in the application of the aerosol beam injector to delivery of molecules to cells". Applicant further goes on to say that, according to Professor Raabe (Attachment 2), the nebulizer of Mets is a model 4207 from Inhalation Plastic Inc., and that this nebulizer operates at a flow rate of about 35 ul/minute per liter of carrier gas. Applicant further says that " in the examples in the Mets patent a carrier gas flow rate of 4 l/minute and a pressure of 30 psi was used in all cases. *That this translates to a sample flow rate of 140 ul/minute* (emphasis added). Under these conditions droplets at the point of impacting target cells were around 2 microns in diameter." Applicant further says that "droplets generated in the Mets nebulizer are large. At the point of impacting cells, they are described as being 2 microns in diameter, or 0.1 microns in Example 2 of Mets." Applicant further says that "*although droplet size at the point of impacting cells was not measured in the current application,* (emphasis added) it is clear the droplet size must be appreciably less than 2 microns since efficient transformation of bacterial cells is reported , E. coli cells are on average 1.5 microns in length and 0.75 microns in width". Applicant further states that "we show that the most effective delivery of molecules to cells occurs at flow rates of between 4.0 and 50.0 ul/minute. Higher flow rates are not a useful and result in significant tissue and cell damage."

Applicant's traversal has been considered and is unpersuasive because the flow rate of Mets is alleged to be 140 ul/min. Applicant 's claims are drawn to 1-350 ul/minute (Claim 1), 1-200 ul/minute (claim 63), 4-50 ul/minute, 8-50 ul/minute, 12-50 ul/minute, and 8-17 ul/minute, ranges which overlap Mets alleged flow rate of 140. Applicant further says that Higher flow rates (than 50 ul/min) are not a useful and result in

significant tissue and cell damage. Yet Applicant claims these higher rates. Applicant is essentially saying that Applicant's claimed ranges are damaging and not functional.

Applicant traverses, stating primarily that Applicant further says that "droplets generated in the Mets nebulizer are large. At the point of impacting cells, they are described as being 2 microns in diameter, or 0.1 microns in Example 2 of Mets."

Applicant's traversal has been considered and is unpersuasive because the droplets of Mets are in the range of 0.1-2.0 microns in diameter. Furthermore, Applicant did not measure droplet size in their experiment.

Applicant traverses, stating primarily that Mets used flow rates that are not optimal and in fact result in extremely low or negligible rates of transformation (Declaration, p. 3), and Applicant is arguing limitations that are not in the claims.

Applicant's traversal has been considered and is unpersuasive because Mets methods produced stable transformants having the specified DNA sequences introduced. Applicant teaches only transient transformation (specification, p.50), which is a far less stringent test of transformation.

Applicant traverses, stating primarily that none of the references cited by the Examiner discloses or suggests using low flow rates with the aerosol beam method of the present invention.

Applicant's traversal has been considered and is unpersuasive because Applicant's arguments are not commensurate in scope with the claim. No claim is drawn to a specific method or apparatus.

Remarks

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 703-308-7023. The examiner can normally be reached on 8:30 - 5:00.

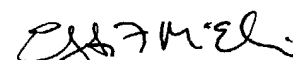
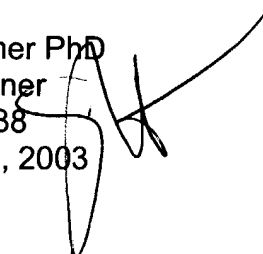
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone numbers for

Art Unit: 1638

the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Georgia Helmer PhD
Patent Examiner
Art Group 1638
November 15, 2003



ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600